

AMENDMENT TO THE CLAIMS:

This listing of claims will replace all prior version and listings of claims in the application:

1. (Currently Amended) A chemically modified ~~double stranded short interfering~~ nucleic acid (siNA) molecule ~~comprising a separate sense strand and antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides~~, wherein:

a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;

[[a.]] b) each strand of the siNA nucleic acid molecule is about independently 18 to about 27 nucleotides in length;

[[b.]] c) an 18 to 27 nucleotide sequence of the antisense strand of the siNA nucleic acid molecule comprises about 18 to about 27 nucleotides that are is complementary to a human amyloid precursor protein (APP) RNA comprising sequence encoded by SEQ ID NO: 1905;

[[c.]] d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid is complementary to the antisense strand and comprises a portion an 18 to 27 nucleotide sequence of the human APP RNA nucleotide sequence of about 18 to about 27 nucleotides;

[[d.]] e) about 50 to 100 percent of the nucleotides positions in each of the sense strand and about 50 to 100 percent of the nucleotides in the and antisense strands of the siNA molecule are chemically modified with modifications independently selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and

[[e.]] f) about 50 to 100 percent of the purine nucleotides in one or both strands of the siNA molecule are 2'-O-methyl purine nucleotides and about 50 to 100 percent of the pyrimidine nucleotides in one or both strands of the siNA are 2'-deoxy-2'-fluoro pyrimidine nucleotides one or more of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2'-O-methyl purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

2. (Canceled)

3. (Currently Amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein ~~the siNA~~ said nucleic acid molecule comprises one or more ribonucleotides.
4. (Canceled)
5. (Canceled)
6. (Canceled)
7. (Canceled)
8. (Canceled)
9. (Canceled)
10. (Canceled)
11. (Canceled)
12. (Canceled)
13. (Canceled)
14. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, one or more of the purine nucleotides present in ~~the~~ said sense strand are 2'-deoxy purine nucleotides.
15. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein ~~about 50 to 100 percent~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the pyrimidine nucleotides present in the sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
16. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends of the sense strand.
17. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.
18. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more ~~about 50 to 100 percent~~ of the pyrimidine nucleotides present in ~~the~~ said antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

19. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more ~~about 50 to 100 percent~~ of the purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides.
20. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, one or more of the purine nucleotides present in the antisense strand ~~comprise~~ are 2'-deoxy-2'-fluoro purine nucleotides.
21. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein the antisense strand ~~comprises~~ includes a terminal phosphorothioate internucleotide linkage at the 3' end of the antisense strand.
22. (Canceled)
23. (Canceled)
24. (Canceled)
25. (Canceled)
26. (Canceled)
27. (Canceled)
28. (Canceled)
29. (Canceled)
30. (Currently amended) The ~~siNA~~ nucleic acid molecule of claim 1, wherein the 5'-end of the antisense strand includes a terminal phosphate group.
31. (Canceled)
32. (Canceled)
33. (Canceled)
34. (Canceled)
35. (Currently Amended) A composition comprising the ~~siNA~~ nucleic acid molecule of claim 1 in a pharmaceutically acceptable carrier or diluent.

36. (New) The nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides.
37. (New) The nucleic acid molecule of claim 1, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides.
38. (New) The nucleic acid molecule of claim 1, wherein the antisense strand, sense strand, or both the antisense strand and sense strand include a 3'-overhang of 1-3 nucleotides.
39. (New) The nucleic acid molecule of claim 38, wherein the nucleotides of the 3'-overhang are chemically modified to comprise one or more phosphorothioate internucleotide linkages, 2'-O-methyl ribonucleotides, 2'-deoxy-2'-fluoro ribonucleotides, 2'-deoxy ribonucleotides, universal base nucleotides, 5-C-methyl nucleotides, inverted deoxyabasic moieties, or a combination thereof.